REMARKS/ARGUMENTS

This Amendment is accompanied by a Declaration under 37 C.F.R. of one of the inventors addressing issues of obviousness over the prior art. Because of the current after-Final proactive, in which an examiner may refuse entry of a declaration if submitted subsequent to a Final Rejection, this Amendment is accompanied by a Request for Continued Examination.

However, should the Examiner find the claims allowable based on this Amendment and the Declaration, Applicants respectfully requests that the Declaration be entered and the Request for Continued Examination not be acted on in light of the allowability of the Application.

Requirement for Restriction

Applicants acknowledge with appreciation the withdrawal of the requirement for restriction as between claims of Groups I and III. However, Applicants submit that the claims of Group II are not directed to an invention different from the elected invention, and request reconsideration of the maintenance of this Requirement.

The Examiner considers that the claims of Group II define a kit that could be used for purposes other than those of Groups I and III, for example, cell separation or purification processes. However, claim 24, the main kit claim, requires that the kit contain one or more "second antibodies" specific to classes or subclasses of modified proteins or to individual modified proteins. Such antibodies would have no use in a kit for cell separation or purification but, on the contrary, would be used in an assay such as a sandwich assay for modified proteins as defined in claims 1 and 36. Retention of claims 24-35 in this Application is respectfully requested.

Rejections under 35 U.S.C. 112

Claim 36 is rejected as vague and indefinite on several grounds.

However, claim 36 is a classic Jepson claim in which a basic type of prior art process is defined in the preamble and a particular inventive feature is defined in the subsequent clause. The language "In a process for ..." and "the step comprising..." indicate these respective

portions of the claim. Applicants consider that the preamble of the claim adequately defines the basic process, namely a process for simultaneously analyzing a sample for a plurality of modified proteins. The specific step is defined as a step for denaturing a plurality of modified proteins (the term "a plurality of" has been added in the event that it is not clear that a plurality of modified proteins, as opposed to a single protein, is denatured in this step, although the use of the plural form "proteins" should already clearly indicate that).

Should the examiner have a different opinion, Applicants would request a specific statement as to why the preamble is inadequate or why the claim is indefinite, and Applicants respectfully request the reasoning for such be set forth.

Rejections for obviousness

Claims 1, 3-16, 21-23, 36 and 37 stand rejected as obvious over Shen et al. in view of Knowles et al. Claim 2 is rejected over the combination of Shen et al., Knowles et al. and Chin et al. Claims 17 and 20 are rejected as obvious over the combination of Shen et al., Knowles et al. and Bayer et al. Claims 18 and 19 are rejected as obvious over the combination of Shen et al., Knowles et al, Bayer et al. and Roser.

Applicants agree with the examiner that Shen et al. disclose a process for simultaneously determining a plurality of modified proteins (i.e., a multiplex assay for such proteins), that Chin et al. disclose arrays of immobilized antibodies, that Bayer et al. disclose the use of the avidin-biotin system in assays and that Roser teaches phycoerythrin conjugates. These all are, indeed, conventional techniques in immunoassays.

Knowles is relied on by the examiner for teaching a denaturation step as claimed herein, and it is with respect to the disclosure of Knowles and its application to the currently clamed multiplex process for analyzing for a plurality of modified proteins that Applicants wish to discuss and to respond.

Knowles et al., as discussed previously, disclose denaturing a single modified glycosylated protein using the detergent SDS (sodium dodecyl sulfate). Knowles et al. disclose that denaturation with a detergent, among which is included SDS, should be carried out at harsher conditions than those claimed - a higher temperature of above 50°C (as opposed to one

between about 4 and about 37°C), a higher concentration of detergent (about 1-3 molar as opposed to 1-10 mM), and a much shorter time (about 1 minute as opposed to about 2 -72 hours). While Knowles et al. disclose that denaturation can be carried out at lower temperatures (i.e. below 37°C) and for longer times (from one to several hours), this procedure is dismissed as being undesirable since the procedure Knowles et al. teach can accomplish the same results in an extremely short time of about 1 minute.

Accordingly, those skilled in the art would not be taught by Knowles et al. to use a shorter time/higher temperature/higher concentration denaturation process. For that reason alone, the claims herein are not obvious over combinations of references in which Knowles et al. is relied on for the denaturation of modified proteins.

In addition, Applicants submit herewith the accompanying Declaration under 37 C.F.R. 1.132 of Quan Nguyen, one of the inventors in this Application. Mr. Nguyen states, in paragraph 6, a number of reasons why those skilled in the art would have considered the denaturation step of Knowles et al. to be unsuitable for a process for analyzing a plurality of modified proteins, i.e. a multiplex process, as opposed to analyzing for a single modified protein.

As stated in the declaration (par. 6) those skilled in the art would know that in a multiplex process, there is a potential for denaturation not only of the modified proteins, but also for partial or complete denaturation of capture antibodies that are added in the same step as the proteins. This certainly would be undesirable. Completely denatured antibodies would not bind to any targets and partially denatured antibodies would become nonspecific. As there are a plurality of antibodies used in multiplex assays, so the possibility for denaturation of some or all would be significantly greater.

SDS, in addition, is generally considered to be too strong a detergent for use in the presence of antibodies. It commonly is used in Western blotting to unfold and linearize proteins. However, in Western blotting, SDS is removed from the system by washing before it would come into contact with any antibodies.

It therefore was surprising that, when used under the claimed conditions, SDS would be suitable for use in denaturing proteins in a multiplex assay.

Applicants submit that for the above reasons the current claims are not obvious over the combination of references, and request that these rejections be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Joel G. Ackerman
Reg. No. 24,307

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
JA:ja
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